REMARKS

Claims 32-39 and 41-47 are now pending for prosecution in this case.

Support for antibody fragments, including antigen binding fragments, appears at least at page 8, lines 7-29. The remaining claims are previously claimed subject manner that has been reorganized in a manner which the Examiner has requested to be a more acceptable Markush format.

The Examiner has indicated that the specification needs to be amended to indicate that the present application is a divisional application of parent application U.S. Patent No. 09/109,207, now U.S. Patent No. 6,172,213.

In response, Applicants respectfully submit that the transmittal submitted on November 17, 2000 did in fact amend the specification to indicate such. However, if the Examiner desires that Applicants submit the amendment again under the revised rules, and cancel the prior transmittal amendment, Applicants will do so. Appropriate clarification and instruction is requested.

The Rejection under 35 U.S.C. § 112, First Paragraph

Claims 32-41 stand rejected under 35 U.S.C. § 112, First Paragraph, as allegedly containing subject matter which is not described in the specification in such a way as to enable one skilled in the art to make and use the invention.

Specifically, the Examiner has indicated that the specification is enabling for combinations of E26 or E27 with an immunosuppressive agent, but not for combinations of an anti-IgE antibody or IgE binding fragment having an aspartyl residue prone to isomerization which has been replaced while retaining at least the same or greater affinity for IgE than the corresponding unimproved antibody or IgE binding fragment.

In response, Applicants' amendments herewith render the Examiner's rejection moot.

The Rejection under 35 U.S.C. § 112, First paragraph

Claims 32-41 stand rejected under 35 U.S.C. § 112, First Paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled that the inventor(s) had possession of the invention.

Specifically, the Examiner has argued that Applicants have not shown possession of the following:

(A) Combinations of an anti-IgE antibody or IgE binding fragment having an aspartyl residue prone to isomerization which has been replaced while retaining at least the same or greater affinity for IgE than the corresponding unimproved antibody or IgE binding fragment;

(B) An immunosuppressive agent comprising an anti-idiotypic antibody which binds MHC antigens or fragments (Claim 34);

(C) An immunosuppressive agent comprising cytokine or cytokine receptor antagonists;

(D) An immunosuppressive agent comprising anti-lymphocyte globulin (Claim 35);

(E) An immunosuppressive agent comprising a soluble peptide containing an LFA-3 binding domain (Claim 36);

(F) An immunosuppressive agent comprising a T cell receptor (Claim 36); and

(G) An immunosuppressive agent comprising a T cell receptor antibodies (Claim 36);

In response, with respect to (A) & (D), Applicants Amendment herewith renders the rejection moot. With respect to (B), (C) and (E)-(G), the Examiner has argued that Applicants have not provided any species, as a result, have not provided a sufficient representative number of species to describe the claimed subgenuses.

Applicants respectfully submit that the Examiner's rejection, especially the reliance upon *University of California v. Eli Lilly*, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997) is misplaced. The salient point of *Lilly* was whether the disclosure of a single species (rat cDNA) provides a written description of the entire genus (mammalian cDNA). That is clearly not the issue here. Applicants are not attempting to claim an entire genus based on only the description of a single species. Applicants' claims are limited to only what has already been described in the detailed description of exemplary immunosuppressive agents at page 12, lines 13-33.

The written description requirement does not mandate that Applicants must describe exactly the claimed subject matter, rather, the only requirement is that the description must clearly allow a person of ordinary skill in the art to recognize that he or she invented what is claimed. *Vas-Cath Inc. v. Mahurkar*, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991). The test is whether the originally filed specification reasonably conveys to a person having ordinary skill in the art that Applicants had possession of the subject matter later claimed. *In re Kaslow*, 217 U.S.P.Q. 1089 (Fed. Cir. 1991). Moreover, the written description guidelines clearly set forth that "the absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 U.S.C. § 112, ¶ 1 for lack of adequate written description." 66(4) *Fed. Reg.* at 1105.

With respect to (B), the words "an anti-idiotypic antibody which binds MHC antigens or MHC fragments" is sufficiently descriptive to one of ordinary skill in the art. It is common practice to define an antibody by the antigen to which it binds. Especially since the immunosuppressory effect follows from the binding to an MHC antigen or fragment thereof, or more specifically, the interference of MHC antigen in the pathophysiology of an immunogenic response, one of ordinary skill can readily identify the claimed

subject matter. As evidenced in Alberts *et al., Molecular Biology of the Cell*, Third Ed., Garland Publishing 1994, the relevant portion of which is hereby submitted in the enclosed Information Disclosure Statement, one of ordinary skill understands and recognizes that MHC antigen or major histocompatibility complex antigen describes a family of cell-surface proteins that bind peptide fragments of foreign proteins and present them to T lymphocytes to induce an immune response.

With respect to (C), one of ordinary skill understands and recognizes a cytokine to be an extracellular signaling peptide or protein that mediates cell-cell communication. In a similar vein, one of ordinary skill understands and recognizes that a cytokine receptor antagonist is a molecule, which interferes or inhibits the binding of a cytokine to a cytokine receptor.

With respect to (E), Applicants have identified that soluble peptides containing LFA-3 binding domains are further defined by the disclosure of WO 90/08187. As mentioned above, the definition of a ligand by the receptor to which it binds is a common method which one of ordinary skill can readily identify the claimed subject matter. It is recognized by one of ordinary skill that LFA-3 stands for lymphocyte-associated function antigen, which is a surface-bound CD2-ligand important in T-cell activation.

Finally, with respect to (F) & (G), T-cell receptor antibodies are further defined by the disclosure of U.S.P. 5, 114, 721, T-cell receptor fragments are further defined in Offner *et al.*, *Science* 251: 430-432 (1991), WO 90/11294 and WO 91/01133 and T cell receptor antibodies are further defined in EP 340,109, with a particular example being T10B9. Thus, in addition to defining the antibody by the target antigen, one of ordinary skill can readily examine the referenced publications to readily identify the claimed subject matter.

The Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 33-36 and 40 stand rejected under 35 U.S.C. § 112, Second Paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention.

In particular, the Examiner has argued that Claims 33-36 are of alleged improper Markush format for containing combinations of subgenuses and species, and for other alleged improprieties of form.

In response, Applicants' amendment herewith renders the rejection moot.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

Applicants believe that this application is now in condition for immediate allowance and respectfully request that the outstanding rejections be withdrawn and this case passed to issue.

The Examiner is invited to contact the undersigned at (650) 225-1489 in order to expedite the resolution of any remaining issues.

Respectfully submitted,

GENENTECH, INC.

By: Craig G. Svoboda

Craig G. Svoboda
Reg. No. 39,044

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the claims:

Claim 40 has been cancelled.

Claims 32-36 have been amended as follows:

32. (Amended). A composition of an improved anti-IgE antibody or IgE binding fragment thereof in combination with an adjunct immunosuppressive agent, wherein the improved anti-IgE antibody or IgE binding fragment ~~has at least one replaced aspartyl residue prone to isomerization replaced and wherein said improved anti-IgE antibody or IgE binding fragment has at least the same or greater affinity for IgE than the corresponding unimproved antibody or IgE binding fragment~~thereof comprises:

(a) the heavy and light chains of E26 (SEQ ID NOs:15-16);

(b) the heavy and light chains of E27 (SEQ ID NOs:17-18); and

(c) antigen binding fragments of (a) or (b).

33. (Amended). The composition of Claim 32 wherein the immunosuppressive agent is selected from the group consisting of ~~2-amino-5-aryl-substituted pyrimidines,~~ azathioprine, cyclophosphamide, bromocryptine and glutaraldehyde.

34. (Amended). The composition of Claim 32 wherein the immunosuppressive agent is a ~~selected from the group consisting anti-idiotypic antibodies which bind MHC antigens or fragments, cyclosporin A,~~ glucocorticosteroids~~, cytokine antagonists and cytokine receptor antagonists~~.

35. (Amended). The composition of Claim 32 wherein the immunosuppressive agent is an antibody selected from the group consisting of: ~~anti-tumor necrosis factor-α; anti-tumor necrosis factor-β; anti-interleukin-2; antibodies; anti-L3T4; anti-lymphocyte globulin;~~ cyclosporin A; anti-CD3; anti-CD4 and anti-CD4a.

36. (Amended). The composition of Claim 32 wherein the immunosuppressive agent is an antibody selected from the group consisting of: a soluble peptide containing a LFA-3 binding domain; streptokinase; TGF-β; streptodornase; deoxyspergualin; rapamycin~~,~~ and T-cell receptor ~~and T-cell receptor antibodies~~.

New claims 42-47 have been added:

42. The composition of Claim 32, wherein the immunosuppressive agent is a 2-amino-5-aryl-substituted pyrimidine.

43. The composition of Claim 32, wherein the immunosuppressive agent is an anti-idiotypic antibody which binds MHC antigens or fragments.

44. The composition of Claim 32, wherein the immunosuppressive agent is a T-cell receptor antibody.

45. The composition of Claim 32 ,wherein the immunosuppressive agent is a cytokine antagonist or cytokine receptor antagonists.

46. The composition of Claim 45, wherein the immunosuppressive agent is selected from the group consisting of: anti-interferon-γ; anti-interferon-β; or anti-interferon-α; anti-tumor necrosis factor-α; anti-tumor necrosis factor-β; anti-interleukin-2; anti-IL-2 receptor antibody and anti-L3T4.

47. The composition of Claim 34, wherein the immunosuppressive agent is selected from the group consisting of: prednisone, methylprednisone and dexamethasone.